



## EDUCATION MODULE

### PRESCRIBING OPIOIDS TO PATIENTS WITH CHRONIC PULMONARY DISEASE\* *(Including sleep-disordered breathing / sleep apnea)*

*This module provides information about chronic pulmonary disease as a risk factor for opioid overdose and specific risk-reduction guidance. It **supplements** but does not replace the general best practices for opioid prescribing presented in the “Considerations for Safe and Responsible Opioid Prescribing” module.*

#### **Background**

1. More than 35 million Americans have a chronic lung disease; asthma is the most common (25 million), followed by chronic obstructive pulmonary disease (15 million), and interstitial lung disease (12 million).<sup>1,2</sup>
  - a. In the U.S., COPD has an estimated prevalence of 14% (this includes an estimated 12 million people who are undiagnosed), and is the third leading cause of death.<sup>3,4</sup>
  - b. The prevalence of diagnosed COPD is highest in persons aged 65 years or older.<sup>4</sup>
2. Approximately 22 million Americans suffer from obstructive sleep apnea (OSA), although 80% of cases of moderate or severe OSA are undiagnosed.
  - a. OSA is more common in men, obese individuals, and with advancing age.<sup>5</sup>
  - b. Opioids cause respiration to slow and become irregular, leading to hypercapnia and hypoxia; in addition, opioids depress hypoxic and hypercapnic ventilator drives.<sup>7</sup>
  - c. Opioids are associated with OSA and central sleep apnea.<sup>6-8</sup>
3. Persons with comorbid COPD and OSA have a worse prognosis than with either condition alone; these patients have more profound hypoxemia (desaturation), more cardiac arrhythmias during apneic events, and an increased likelihood of pulmonary hypertension.<sup>4</sup>

#### **Chronic pulmonary disease and opioid overdose**

1. Opioids can cause respiratory depression by depressing the central nervous system (CNS), including the medullary respiratory center that controls respiratory ‘drive’ with input from peripheral chemoreceptors.
  - a. This results in decreased respiratory rate, tidal volume, inspiratory pressure, and ‘central apnea,’ which are especially dangerous in persons with obstructive or central sleep apnea, other chronic pulmonary conditions (e.g., COPD), and at high opioid doses.<sup>7,9</sup>
  - b. Patients with COPD and sleep apnea who are prescribed opioids are at higher risk for opioid-related toxicity/overdose and overdose-related death.<sup>10,11</sup>



- c. In patients with severe COPD and baseline pCO<sub>2</sub> elevations, opioid use carries the risk of increasing their narcotizing effect by encouraging further CO<sub>2</sub> retention.<sup>12</sup>
2. The risk of respiratory depression increases after 60 years of age.
  - a. Age-related changes in the respiratory system that reduce the ability to tolerate opioid-induced respiratory depression include decreased sensitivity of central and peripheral chemoreceptors to hypercapnia and hypoxia, and diminished compensatory respiratory drive.<sup>4,13,14</sup>
  - b. Older patients with COPD commonly have co-occurring coronary heart disease, heart failure, OSA, asthma, or stroke, which also increase the risk of opioid-induced respiratory depression.<sup>4,10-12,15,16</sup>
  - c. Smoking is common (28% to 54%) in people with chronic pain.<sup>17-19</sup>

### **Risk-mitigating interventions to consider when prescribing opioids for patients with chronic pulmonary disease**

[Refer to the full prescribing information (see: **FDA Label**) for important product-specific details]

1. Optimize the medical management of underlying pulmonary disorders and any co-occurring chronic pain and mental health conditions. Encourage the patient to quit smoking.
2. Avoid initiating opioids during acute exacerbations of COPD.<sup>20</sup>
3. Screen patients with COPD for OSA.<sup>21-23</sup>
4. Avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible.<sup>7</sup> Use close monitoring and cautious dose titration if opioids are prescribed for patients with mild sleep-disordered breathing.<sup>22</sup>
5. Avoid concurrent use of other medications or substances that are central nervous system depressants such as benzodiazepines, sedatives/hypnotics, and alcohol in opioid-treated patients with chronic pulmonary disease or moderate-to-severe OSA. These combinations can result in profound sedation, respiratory depression, coma, and death; they should be restricted to the minimum required dosage and duration in patients for whom alternative treatment options are inadequate.<sup>20-22,24</sup> (see also: **FDA Label**)
6. Closely monitor opioid-treated patients with chronic pulmonary disease for respiratory depression and over-sedation, particularly during initiation and after dosage escalations. The risk for overdose is greatest during the first 3 to 7 days after starting an opioid or increasing its dosage. This occurs because tolerance to an opioid's respiratory depressant effects is slower to develop and less complete than tolerance to its analgesic or euphoric effects.<sup>22,25-27</sup>



7. Consider prescribing take-home naloxone to patients with chronic pulmonary disease to reverse life-threatening respiratory depression if an overdose occurs. Educate the patient, family/household members, and caregivers about signs and symptoms of opioid overdose and train them to properly use naloxone if an opioid-related overdose is suspected.<sup>22,28</sup>
8. Consider consultation or co-management with a specialist in pain medicine and/or pulmonary medicine when prescribing opioid analgesics in patients with chronic pulmonary disease or sleep-disordered breathing.<sup>22</sup>
9. For patients who have severe, end-stage COPD with refractory dyspnea, opioid therapy may be considered as adjunctive therapy when conventional management is insufficient.
  - a. Conventional management for dyspnea includes short- and long-acting bronchodilator therapies, inhaled corticosteroids in combination with long-acting beta-2-agonists, theophylline preparations, as well as nonpharmacologic therapies such as pulmonary rehabilitation and breathing/relaxation techniques.<sup>4,29,30</sup>
  - b. Use particular caution in patients who are opioid-naïve or not opioid-tolerant. (see also: **FDA Label**)
    - i. Adults are considered opioid-tolerant if they have been receiving a total daily opioid dose equivalent to at least 60 mg of oral morphine (60 MME/day) for one week or longer.<sup>31</sup> (See 'Treatment' section 3a in the "**Considerations for safe and Responsible Opioid Prescribing in Adults**" module)
      - 60 mg oral morphine per day
      - 25 mcg transdermal fentanyl per hour
      - 30 mg oral oxycodone per day
      - 60 mg oral hydrocodone per day
      - 8 mg oral hydromorphone per day
      - 25 mg oral oxymorphone per day

### **Additional Resources**

*\*The information presented in this module highlights some fundamental concepts of opioid prescribing for adult outpatients. It excludes certain populations (pediatrics, pregnancy, patients with active cancer or receiving palliative or end-of-life care) and settings (perioperative, emergency, in-patient). The information provided is intended to support safe and effective opioid therapy and minimize serious adverse outcomes, particularly overdose. It is not intended to be exhaustive nor substitute for consulting a medication's full prescribing information for complete details and warnings. Links and references to selected, more comprehensive clinical and prescribing resources are provided to facilitate safe and effective opioid prescribing.*

1. **FDA-approved drug label information:** [FDA Online Label Repository](#) or [Daily Med](#) (NIH/National Library of Medicine)
2. [American Thoracic Society Guidelines](#)
3. [American Academy of Sleep Medicine Practice Guidelines](#)

## References

1. Blackwell DL, Lucas JW, Clarke TC. Summary health statistics for U.S. adults: National Health Interview Survey, 2012. National Center for Health Statistics. *Vital Health Stat* 2014;10(260). PMID: [24819891](#)
2. Wheaton AG, Cunningham, TJ, Ford ES, Croft JB. Employment and activity limitations among adults with chronic obstructive pulmonary disease—United States, 2013. *MMWR*. 2015;64(11):290-295. PMID: [25811677](#)
3. National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI). Morbidity and mortality: 2012 chart book on cardiovascular, lung and blood diseases. Bethesda, MD: [NHLBI 2012](#).
4. [GOLD 2018](#): Global Strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. <http://goldcopd.org/gold-reports/>
5. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. *Sleep Medicine Reviews* 2017;34:70-81. PMID: [27568340](#)
6. Pattinson KT. Opioids and the control of respiration. *Br J Anaesth* 2008;100:747-58. PMID: [18456641](#)
7. Correa D, Farney RJ, Chung F, Prasad A, Lam D, Wong J. Chronic opioid use and central sleep apnea: a review of the prevalence, mechanisms, and perioperative considerations. *Anesth Analg*. 2015;120(6):1273-85. PMID: [25988636](#)
8. VanRyswyk E, Antic NA. Opioids and sleep disordered breathing. *Chest* 2016;150:934-944. PMID: [27262224](#)
9. Yamanaka T, Sadikot RT. Opioid effect on lungs. *Respirology*. 2013 Feb;18(2):255-62. PMID: [23066838](#)
10. Zedler B, Xie L, Wang L, et al. Risk factors for serious prescription opioid-related toxicity or overdose among veterans health administration patients. *Pain Med*. 2014;15:1911-1929. PMID: [24931395](#)
11. Nadpara PA, Joyce AR, Murelle EL, et al. Risk factors for serious prescription opioid induced respiratory depression or overdose: Comparison of commercially insured and veterans health affairs populations. *Pain Medicine* 2018;19:79-86. PMID: [28419384](#)
12. Albertson TE, Schivo M, Zeki AA, et al. The pharmacological approach to the elderly COPD patient. *Drugs Ageing* 2013;30:479-502. PMID: [23580319](#)
13. Cepeda MS, Farrar JT, Baumgarten M, et al. Side effects of opioids during short term administration: Effect of age, gender, and race. *Clin Pharmacol Ther* 2003;74:102-12. PMID: [2891220](#)
14. Davies GA, Bolton CE. Chapter 15. Age related changes in the respiratory system. In: Fillit HM, Rockwood K, Woodhouse K, eds. *Brockelhurst's Textbook of Geriatric Medicine & Gerontology*, 7<sup>th</sup> ed, 2010.
15. Hernandez P. Chapter 48. Asthma and chronic obstructive pulmonary disease. In: Fillit HM, Rockwood K, Woodhouse K, eds. *Brockelhurst's Textbook of Geriatric Medicine & Gerontology*, 7<sup>th</sup> ed, 2010.
16. Wheaton AG, Ford ES, Cunningham TJ, Croft JB. Chronic obstructive pulmonary disease, hospital visits, and comorbidities—National Survey of Residential Care Facilities, 2010. *J Aging Health*. 2015;27:480-499. PMID: [25288588](#)

17. Goesling J, Brummet CM, Meraj TS, et al. Associations between pain, current tobacco smoking, depression, and fibromyalgia status among treatment seeking chronic pain patients. *Pain Med* 2015;16:1433-1422. [PMID: 25801019](#)
18. Orhurhu VJ, Pittlekow TP, Hooten WM. Prevalence of smoking in adults with chronic pain. *Tobacco Induced Diseases* 2015;13:17. [PMID: 26185492](#)
19. Plesner K, Jensen HI, Hojsted J. Smoking history, nicotine dependence, and opioid use in patients with chronic pain. *Acta Anaesth Scand* 2016;60:988-994. [PMID: 27166121](#)
20. Vozoris NT, Wang X, Fischer HD, et al. Incident opioid drug use among older adults with chronic obstructive pulmonary disease: a population-based cohort study. *Br J Clin Pharmacol*. 2016 Jan;81(1):161-70. [PMID: 27418553](#)
21. Busse J, Craigie S, Juurlink D, et al. Guideline for opioid therapy and chronic noncancer pain: Appendix. *CMAJ* 2017. [PMID: 26461074](#)
22. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016. *MMWR Recomm Rep*. 2016;65(1):1-49. [PMID: 26987082](#)
23. U.S. Department of Veterans Affairs. VA/DoD clinical practice guideline for opioid therapy for chronic pain. Washington, DC: US Department of Veterans Affairs; 2017. [Guidelines](#)
24. Vozoris NT, Stephenson AL. Benzodiazepine drug use and adverse respiratory outcomes among older adults with COPD. *Eur Respir J*. 2015 Feb;45(2):566-7. [PMID: 25653272](#)
25. Washington State Agency Medical Directors' Group ([WAMDG 2015](#)). Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An Educational Aid to Improve Care and Safety With Opioid Treatment. Corvallis, WA: Washington Department of Health, 2015.
26. Dumas EO, Pollack GM. Opioid tolerance development: a pharmacokinetic/pharmacodynamic perspective. *AAPS J*. 2008;10:537-51. [PMID: 18989788](#)
27. White JM, Irvine RJ. Mechanisms of fatal opioid overdose. *Addiction* 1999;94:961-72. [PMID: 10707430](#).
28. [FSMB 2017](#): Federation of State Medical Boards. Guidelines for the Chronic Use of Opioid Analgesics. April 2017. [https://www.fsmb.org/globalassets/advocacy/policies/opioid\\_guidelines\\_as\\_adopted\\_april-2017\\_final.pdf](https://www.fsmb.org/globalassets/advocacy/policies/opioid_guidelines_as_adopted_april-2017_final.pdf)
29. Ekstrom M, Nilsson F, Abernethy AA, Currow DC. Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. *Ann Am Thorac Soc*. 2015;12(7):1079-92. [PMID: 25803110](#)
30. Mularski RA, Rocker G. Managing dyspnea in advanced chronic obstructive pulmonary disease: Balancing all the evidence. *Ann Am Thorac Soc* 2015;12:978-80. [PMID: 26203609](#)
31. FDA REMS. Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. May 2017. [FDA Blueprint 2017](#)